Q.1 Compare

Primary Systemic Amyloidosis & Primary Cutaneous Amy.

	1ry Cutaneous Amyloidosis	1ry Systemic Amyloidosis
Pathogenesis	Theories - Prolonged Friction - genetic Predisposition - Epstein-barr virus	- plasma cell Dyscrasia (multiple myeloma)
ystemic affects	Absent	Present wide Spectrum of organs affects
mmunofluoresct	Anti keratin Antibodies +ve	-ve
CP	I- papular amyloidosis. - Shins of tibia brown-red Scaly with Severe Pruritus. II Macular amyloidosis - upper back + inter Scapular region - Moderet pruritis. III - Nodular Amyloidosis - No Pruritis - Yellowish waxy nodules	I Muco-cutaneous → Skin - waxy papules, nodules or plaques. - infiltrate of blood vessels → Periorbital (Racoon eye) sign → on eye lid, axilla, genital. → oral Cavity - Macroglossia (Tongue enlarg - Xerostomia (salivary glan II feature of multiple myeloma. → Bone Pain, fracture. → Bense-Jones Proteinuria. → Bone marrow → Atypical plasma cell III Systemic Affection

Q1

2

	1st Cutaneous	1st Systemic
		→ Non specific Symptoms.
		→ organ affection:
		① heart → Congestive heart failure. Cause of Death.
		② Renal failure.
		③ gastrointestinal bleeding.
		④ Abdominal pain.
Histopathology	→ Macular Amyloidosis. (degeneration of basal cells) → deposit in upper dermis	→ Skin lesion. deposit of amyloid around wall of blood vessels. - ① Dermis around fat
	→ Lichen Amyloidosis. → degeneration of basal cell + reactive acanthosis + hyperkeratosis.	→ of no Skin lesion → Rectal Biopsy → +ve G → non involved skin +ve
	→ Nodular Atopic epidermis. + Deposit of Amyloid into Subcutaneous & Blood vessel wall.	
Treatment	- Potent topical Corticosteroids. - intralesional Corticosteroid - Phototherapy - Co_2 laser - Dermabrasion - Excision in nodular type	- cytotoxic Drugs (Melphalan) Steroids

diagnostic criteria of L Amyloidosis

Q2 metabolic ①

Lichen amyloidosis = papular amyloidosis

- The most common type of Iry localized cutaneous Amyloidosis
- more common in male than female

Site → shin of the tibia « most common site » may occur in forearm, thigh or any where

Diagnostic Criteria

CIP

- Papules → Severe pruritic « itchy »
  discrete, closely seated
  hyperkeratotic, slightly scaly
  Brown to red colour
- papules may colasice together and make Thickened plaque

Skin biopsy

Stained by

① Congo red stain

By polarized light ⟹ « Apple green birefringence »

By light microscope ⟹ « orange red colour »

② Haematoxlin / eosin ⟹ « Amorphus eosinophilic masses »

Q2 metabolic

③ other stains → Methyl Violet ، PAS stain
Crystal violet ، pagoda red

Histopathology

epidermal → ACanthosis ، hyper-keratosis
epidermal hyper-plasia

dermal → Amyloid deposit in dermal papillae

Differential diagnosis

- lichen simplex chronicus ⟩ at shine of the tibia
- hypertrophic lichen planus ⟩
- papular mucinosis
- pretibial myxedema
- prurigo nodularis

NB) نقاط على شرح

- pt ē lichen amyloidosis may also has macular Amyloidosis
- Type of Amyloid in lichen Amyloidosis is « Amyloid K »

K → From Keratinocyte

degeneration of Basal KCs
Keratin filaments → Amyloid

- Amyloid deposition in lichen Amyloidosis

deposited at upper dermis

Q4 | Reticular erythematous Mucinosis ? H/P, D.D, Management

Management include c/p, investigation & Tt

- **C/P** Asymptomatic, reticulated arrays "net like" على شكل شبكة
  well defined irregular Margins in mid line of chest or upper back, UV → exacerbate the condition

H/P special stain for cutaneous Mucin:
- Colloidal iron → blue green
- Alcian blue → +ve at PH 2.5
- Toluidine blue → Metachromasia at pH 7 & 4
- PAS -ve

in REM → upper Dermis show - Mucin deposition between Collagen bundles
- Vascular Dilatation
- perivascular Mononuclear infiltration

DIF :- IgM Deposition along basal layer.

D.D
1. Scleredema → No inflammatory infiltrate
2. SLE & SCLE → differentiated clinically & H/P & serologically
3. Polymorphus Light eruptions
4. Pseudo lymphoma - Jessner lymphocytic infiltration -
5. MF
6. Seborrheic D.
7. Psoriasis
8. Acne
9. Eczema
10. Lichen sclerosis
11. Erythema caused by Cardiac pacemaker
12. Photosensitive dermatosis ex Solar Dermatoses, active Dermatoses

Tt :- Anti Malarials : Hydroxychloroquine - 2-6 wks
- Sun screen
- UVA irradiation
- UVB irradiation
- Topical Steroids, Topical Tacrolimus
- systemic steroids, Cyclosporin, Tetracycline, Antihistamines

5Q Metabolic process of porphyrin & each disease caused by it

—

Glycine + succinyl CoA

↓ Aminolaevulinic acid synthase 2 (ALA)

Delta Aminolaevulin acid.

↓ ALA dehydratase

Prophobilinogen

↓

~~porphobilinogen~~

Hydroxymethylbilinogen.

↓

Uroporphyrinogen → uroporphyrin I & III

↓

Coproporphyrinogen → Coproporphyrin I and III

↓ Coproporphyrinogen oxidase

protoporphyrinogen IX

↓ protoporphyrinogen oxidase

protoporphyrin IX

↓ ferrochelatase + Fe^{2+}

Heme + Globin + Apoprotein

↓ ↓

Hemoglobin Cytochromes

Dises

Diseases

① X-linked dominant porphyria — Caused by deficiency of Aminolaevulinic acid (ALA) synthase 2

② ALA dehydratase enzyme deficiency — Caused by ALA dehydratase deficiency

③ Acute intermittent porphyria
- → AD
- → due to deficiency of prophobilinogen deaminase

④ Congenital erythropoietic porphyria
- → AR
- → Caused by deficiency of uroporphyrinogen III synthetase

⑤ Porphyria cutanea tarda.
- → due to deficiency of uroporphyrinogen III decarboxylase

⑥ Hepatoerythropoietic porphyria.
- → AD
- → ↓↓ of uroporphyrinogen oxidase.

⑦ Hereditary Coproporphyria
- → AD
- → ↓↓ of Coproporphyrinogen oxidase

⑧ Variegate porphyria.
- → AD
- → ↓↓ of protoporphyrinogen oxidase.

⑨ erythropoietic protoporphyria
- → AD
- → ↓↓ ferrochelatase enzyme

☆ Metabolic ☆

(1)

Q6 (M.6):-
Etiology, clinical features, diagnosis & TTT of porphyria cutanea tarda?

1. Etiology:- Deficiency of the uroporphyrinogen decarboxylase (UROD) enzyme leading to accumulation of uroporphyrin.

2. Clinical features:- ▪ Fragility & blistering of exposed skin, ▪ Minor trauma to the hands causes sharply marginated erosions.
▪ Bullae occur & may be painful. They crust & resolve over a few weeks leaving atrophic scars, milia & often mottled hyper or hypopigmentation.
▪ Patches of scarring alopecia (after scalp bullae).
▪ Hypertrichosis of the face.
▪ Melasma-like hyperpigmentation ▪ Photo-induced onycholysis.
▪ Morphea-like plaques on the head & upper trunk.

3. Diagnosis:- ▪ History taken. (family history) Genetic in 20% of pt.) & 60% of pt. have liver dz.
▪ Clinical picture. ▪ Histopathology:-
(1) Homogenous material is seen within vessel walls of the upper dermal & papillary vascular plexus
(2) Its PAS+ve, diastase resistant & contains: protein polysaccharide complex, lipids & tryptophan.
(3) IF → immunoglobulins (mainly IgG) in the same vascular distribution & OED.
(4) Bullae are subepidermal split occuring in the lamina lucida leaving the dermal papilla protruding into the bilster cavity (Festooning).

5. CBC & Hb level. 6. Liver enzymes.
7. PCR (for hepatitis C patients)

(8) Treatment:- 1. Opaque Sunscreens.
2. Stop of alcohol or estrogen therapy to prevent exacerbation of the disease
3. Treatment of hepatitis C if present.
4. There are 2 specific therapies for PCT:-
[A] Low-dose antimalarials (chloroquin) is very effective & it the treatment of choice.
Dose:- 125-250 mg/twice/week (clinical remission within 6 months & biochemical after 6-15 moths).
- Hydroxy chloroquine (200mg twice/week) can be used but duration of remission is shorter.
[B] Venesection:- Around 500 ml of blood are removed every week or every 2 weeks.

« porphyria Cutanea tarda » (PCT)

Q: PCT (etiology / CP / Diagnosis / investigation / treatment)

Q: Mention The defect in: PCT

Q: Pseudoporphyria

Q: Compare - PCT & CEP
- PCT & Pseudoporphyria.

- Incidence: Most Common Form of porphyrias.
- Deficient enzyme: (Uroporphyrinogen III decarboxylase)
- Mode of inheritance:
  - (a) Familial PCT → inherited as AD trait
    - → The enzyme is deficient → in The → liver, → erythrocytes, → other tissues
  - (b) Sporadic PCT → inherited as AR trait
    - → The enzyme is deficient → in The → Liver (Only)
    - → require The association of hepatic siderosis.
- Classification:
  - Cutaneouse
  - Non-acute
- Clinical Features
  - (a) Precipitating factors — Liver اذا أثرت على الـ (AB SHEO)
    - (1) Alcoholism
    - (2) Chronic liver disease
    - (3) chronic Liver intoxication → By (Drugs) e.g.
      - A → Arsenic
      - B → Barbiturates
      - S → Steroid
      - H → Hydantoins
      - E → estrogen
      - O → oral Contraceptive pills
    - (4) Exogenouse chemical exposure e.g. Hexa Chlorobenzene.
    - (5) Hepatoma
    - (6) Carcinoma metastasis to the Liver.
    - (7) Systemic LE, Dermatomyositis and AIDs may be associated with PCT
    - (8) In patients with Chronic renal Failure receiving hemodialysis

PCT-Like picture → may occur with normal porphyrin Level → pseudo PCT (تشبه clinically PCT لكن القيم normal)

However → a marked increase ↑↑ in plasma, urinary & Fecal porphyrins may occur in These patients → Pseudo-Pseudo PCT

(Clinical Features) → in Starts in Middle age

Skin Lesions

- (a) Signs of photosensitivity
  - → Vesicles & bullae
  - → on exposed areas as → Face, → dorsa of hands
  - → That rupture → erosions & ulcerations
- (b) Hypertrichosis
- (c) Hyper pigmentation
  - } → of Face, neck, Hands
- (d) Pseudo-scleroderma → The skin of The Face & dorsa of hands is Thickened & sclerotic

Liver

- Mild hepatic cirrhosis with siderosis
- even malignant hepatoma

« cirrhosis → Sidrosis → hepatoma »

- Histopathology → فاضلة
- Investigations (Laboratory findings)
  - (1) Urine
    - ↑ Uroporphyrinogen III → (uroporphyrins III)
    - The urine is brown — بف (قبل ما نعمله) with Continouse Coral pink flurescence under wood's light.
  - (2) Stool — ↑ iso Coproporphyrin & Coproporphyrin.
  - (3) Erythrocytes — Normal.

- DD
  - (1) Other types of cutaneouse porphyria That manifest with Blistering e.g.
    - → Mild variants of CEP & HEP
    - → VP & HCP → /// More important, They Can be associated with Life Threatning acute attacks
  - (2) Pseudo porphyria.
  - (3) Epidermolysis bullosa acquisita
  - (4) Polymorphous light eruption.
  - (5) Phototoxic & Bullous Drug eruption.

  } → All These diseases Can be differentiated from porphyria → By porphyrin analysis

Pseudoporphyria Q 8 ① metabolic

pseudoporphyria « pseudoporphyria Cutnea tarda.
بدل ! سماه كدا
bullous dermatosis of dialysis

→ it is a condition resemble PCT But ̄c out Biochemical abnormalites in porphyrin metabolism « Normal porphyrin metabolism »

C/P Skin Fragility
erosions
vesiculo bullous leion c scaring } sun exposed area

(ct) Face c dorsum of the hands
extensor surface of the legs c foots

Causes c triggre factors

① chronic renal failur pt ̄c renal dialysis
② drugs « make photo sensitivity »
- . NSAID → Ketoprofen c naproxen
- . Fruosmide c tetracylin
- . Doxcylin c retinoids

③ Taning beds اجهزة التشمس
palm vesicles الاف متعرفة.

labrotory Blood c stool c urine Free

Histopathology same As PCT

Q8 (2) metabolic

HP → . Subepidermal cell poor blister
. minimal inflamtory infiltrate
. Charactristic Festooning of dermal papillae due to deposition of PAS +ve glycoprotein in and around the wall of the vessels localized in upper dermis

DD

Porphyria Cutena tarda
Epidermolysis Bullosa
Epidermolysis Bullosa aquistica
Bullous pemphigoid

tt

. if drug induced → stop the drug
. Sun protection
. Sun screen

Xanthomatosis

- Xanthomas are reactive yellowish tumors composed of masses of lipid-containing histiocytes.
- They denote the presence of elevated blood lipids, lipoproteins, atherosclerosis & even fatal cardiovascular disease.

Clinical varieties

1. ***Tuberous xanthomas*** (Figs 38-42): Appear as slowly developed, firm yellow, or orange grouped papules & nodules symmetrically distributed on elbows, knees, hands, feet & buttocks. They are seen with increased levels of β-lipoproteins (LDL) in familial hypercholesterolemia (FH) (Type II), broad beta disease (Type III) & in 2ry hyperlipidemia as hypothyroidism & chronic biliary disease. Atherosclerosis is frequently seen in these patients.

Fig. 38. Tuberous xanthomas

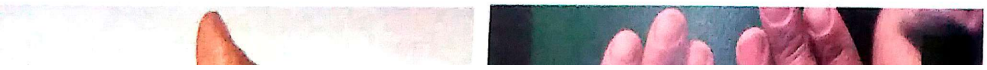
2. ***Tendinous xanthomas*** (Figs 43-46): Appear as slowly enlarging, smooth, and firm subcutaneous nodules attached to tendons, ligaments and fascia of the hands, knees elbows and achilles tendons.

They are seen with increased levels of beta-lipoproteins (LDL) in FH (Type II), broad beta disease (Type III), and obstructive liver disease. Atherosclerosis is commonly seen.

Rarely, tendinous xanthomas can develop in the absence of a lipoprotein disorder.

Two examples are:

- Cerebrotendinous xanthomatosis: An enzymatic defect exists in the bile acid synthetic pathway, leading to the abnormal accumulation of an intermediate known as cholestanol. This intermediate is deposited in most tissues, including the brain, and can also form tendinous xanthomas.
- β-sitosterolemia: An abnormal accumulation of plant sterols occurs, leading to tendinous xanthoma formation.



3. ***Eruptive xanthomas*** (Figs 47-50):
   - Appear as small, asymptomatic, yellow papules with an erythematous base. They appear suddenly mainly on the buttocks, shoulders and extensor surfaces of extremities.
   - They are seen with hypertriglyceridemia and a high conc. of chylomicrons & VLDL (Type I, IV & V). They are also seen in 2ry hyperlipidemias, e.g. DM, pancreatitis & hypothyroidism.
   - *DD:* Xanthoma disseminatum: Occurs in normolipemic patients; red-yellow papules with flexural predilection.

4. ***Plane xanthomas:*** Appear as yellow, soft macules or slightly elevated plaques of which many types are known:
   - *Xanthelasma "xanthelasma palpebrarum"* (Figs 51-58): Occurs mainly on the medial portion of the upper eyelids. It is suggestive of increase in LDL in type II or III hyperlipoproteinemias or in chronic biliary obstruction. However, in 50% of the patients, no plasma lipoprotein elevations could be detected.

- *Xanthoma palmaris* (Figs 59-62): Appears as flat yellow linear lesions in the creases of the palms and fingers. They are pathognomonic of elevation in IDL in type III hyperlipoprotinemias.

- ***Tuberous xanthomas*** (Fig. 64): Demonstrate large aggregates of foam cells in the dermis and fibrosis but without a large number of inflammatory cells.
- ***Tendinous xanthomas:*** Have a similar histology but the foam cells are even larger in size.
- ***Plane xanthomas*** (Fig. 65): The foam cells are more superficial than in other types of xanthomas. The lesions are noninflammatory and have minimal fibrosis.
- ***Verruciform xanthomas*** (Fig. 66): Show hyperkeratosis, acanthosis, papillomatosis and foamy macrophages limited to the submucosa or dermal papillae.

- Generalized plane xanthomas: Extensive yellow infiltrative lesions that diffusely involve face, neck, upper trunk and arms. It is observed in association with various paraproteinemias (myeloma, lymphomas, cryoglobulinemias, macroglobulinemia) with or without hyperlipoproteinemia.

5. Verruciform xanthomas

- Asymptomatic, planar or verrucous solitary plaque, 1 to 2 cm in diameter.
- They occur primarily in the mouth, but sometimes in anogenital (including the scrotum) or periorificial sites.
- There is usually no associated hyperlipidemia and the lesions persist for years.
- These lesions are also seen in the setting of lymphedema, epidermolysis bullosa, pemphigus, discoid lupus erythematosus, GVHD & CHILD syndrome.

Histopathology

Xanthomas are characterized by the presence of xanthoma or foam cells, which are macrophages filled with phagocytosed lipid droplets, and as lipid droplets have dissolved during processing on routine staining the cytoplasm appears foamy. Lipid droplets can be stained with fat stains as scarlet red or Sudan red. In addition, there are Touton giant cells, which are multinucleated with the nuclei grouped in the center around a small island of non-foamy cytoplasm and surrounded by foamy cytoplasm. Polarized microscopy can be used to detect lipid material in the dermal infiltrates, as cholesterol esters are doubly refractile.

- ***Eruptive xanthomas*** (Fig. 63): Contain lipid deposits in the reticular dermis. The initial inflammatory infiltrate is mixed, containing both neutrophils and lymphocytes. Extracellular lipids are present in the dermis.

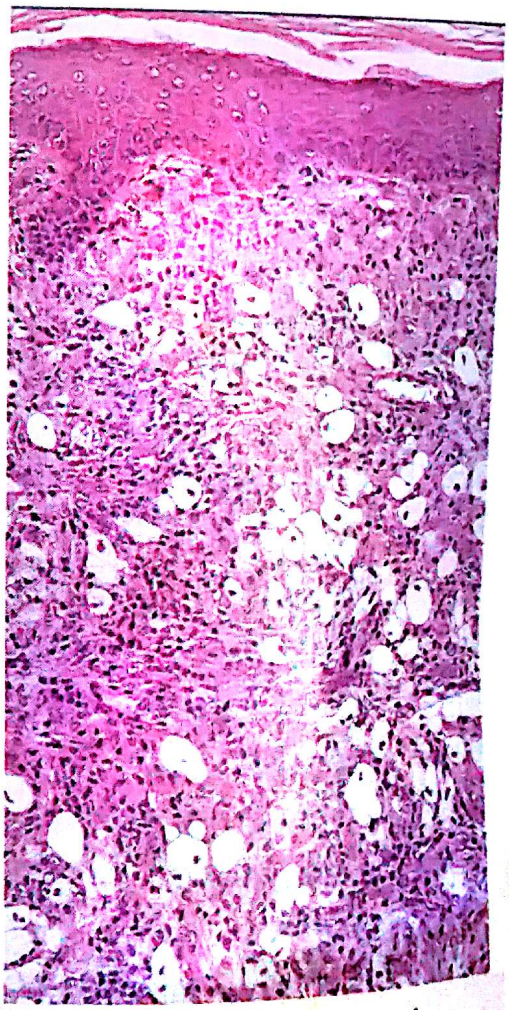


Fig. 63. Histopathology of

Treatment of xanthomas

The treatment of xanthomas associated with hyperlipidemia

- Dietary control.
- Lipid lowering drugs.

Indications

- Patients with hypercholesterolemia to prevent development or progression of atherosclerosis.
- Patients with severe hypertriglyceridemia to prevent acute pancreatitis.

Treatment of skin lesions

- Surgical excision.
- Destructive methods: Laser surgery (CO_2, pulsed-dye or erbium:YAG lasers), chemical agents such as trichloroacetic acid, and cryosurgery.

Indications

- Tendinous or tuberous xanthomas producing pain or disability.
- Xanthelasma without hyperlipoproteinemia causing cosmetic disfigurement.

Normolipidemic xanthomatosis

Xanthomas can arise in the absence of elevated blood lipids or lipoproteins.

I) **Local lipid metabolism disturbances: Which may be related to local tissue abnormalities as inflammation in the skin, which increase vascular permeability of lipoproteins, e.g.:**
   - Xanthelasmas, although not preceded by inflammation.
   - Xanthoma disseminatum.
   - Diffuse normolipemic plane xanthoma.
   - Necrobiotic xanthogranuloma.
   - Xanthomas occurring in atopic dermatitis, epidermolysis bullosa, and erythroderma.

II) **Altered lipoprotein content or structure:**
   e.g. unusual lipids accumulating in lipoproteins.
   - Cerebrotendinous xanthomatosis with accumulation of **cholestanol** in plasma and tissues e.g. skin, heart, brain.

III) **Lymphohistiocytic proliferation in skin with secondary deposition of lipids in cells:**
   - Myeloma.
   - Waldenstrom's macroglobulinemia.
   - Cryoglobulinemia.
   - Lymphomas.

Q 13

Normolipidemic Xanthoma ?

Def Xanthoma arise in ~~absence~~ absence of elevated blood lipids or lipoproteins

Causes

1) Local lipids Metabolism disturbance
→ may due to local tissue abnormalities or inflammation → ↑ Vascular permeability of lipoproteins

e.g
- Xanthelasma
- xanthoma dissemenatum
- Diffuse normolipidemic Xanthoma
- Necrobiotic Xanthogranuloma
- Xanthoma on Top of Atopic dermatitis, Bullosa, erythroderma

2-) Altered lipoprotein Content or structure

e.g unusual lipid accumulating in lipoproteins
→ Cerebrotendinous xanthomatosis → accumulation of Cholestanol in plasma & tissue e.g skin, brain, heart

3) lymphocytic proliferation in Skin & 2ndry deposition of lipids in cells
- Myeloma
- lymphomas
- Cryoglobulinemia
- waldenstroms macroglobulinemia

4) Drug induced tuberous or tendinous Xanthoma

H/P All xanthoma types show foam cells Histiocytoge Contains lipid droplets - Touton Giant Cells - Multinucleated cells & nuclei centrally arranged around an foamy cytoplasm surrounded by foamy cytoplasm

in Drugs
→ ↓ of underlying Cause or defect
Local lesion → excision, cryosurgery, laser : Co, pulsed dye, erbium Yag laser

Q(14) Clinical types & association of Cutaneous Xanthoma

① Definition:

Xanthoma are reactive yellowish tumors composed of masses of lipid containing histiocytes.

denoting the presence of elevated blood lipids lipoproteins, atherosclerosis & even cardiovascular disease

② Clinical Varities:

(a) Tuberous Xanthoma:

* firm yellow slowly progressing grouped papls & nodules symmetrically distributed on elbows, knees hands, feet buttocks.

* Caused by → increased level of Familial hypercholesterolemia

Type II

→ broad beta disease type III

(b) Tendinous Xanthoma:

* appear as [slowly growing enlarging smooth & firm subcutaneous nodules attached to tendons, ligaments & fascia of the hands, knee, elbows and achilles tendon

* Caused by → increased levels of beta lipoproteins (LDL) in familial hypercholesterolemia type II

(3) Eruptive xanthoma.

- Small, asymptomatic, yellow papules with an erythematus base.
- appear on buttocks, shoulders & extensor surface of extremities.

Caused by → hyper-triglyceridemia
& high levels of Chylomicrons.
& VLDL (type I, IV, V)
also seen in 2ry hyperlipidemia.
e.g DM, pancreatitis.

(4) Plane xanthoma.

- yellow, soft macules or slightly elevated plaques of which many types are known

* Xanthelasma → occur mainly on the medial portion of upper eyelids.
- suggestive of increased level of LDL in type II or III hyperlipoproteinemia

* Xanthoma palmaris -
- flat yellow linear lesions in the creases of the palms & fingers
- pathognomic of elevated "IDL" in type III hyperlipoproteinemia

* Generalized plane xanthoma -
- extensive yellow infiltrative lesions that usually involve face, neck, upper-trunk
- observed in association of myeloma, lymphoma

⑤ Verruciform Xanthoma.

- asymptomatic, planar or verrucous solitary plaque
- occur primarily in the mouth but sometimes in anogenital or periorificial sites.
- usually no associated hyperlipidemia
- lesions persist for years.
- lesions also seen in
  - lymphedema.
  - epidermolysis bullosa
  - pamphigus

⑥ Normolipidemic Xanthomasis

- occur in absence of elevated blood lipids.
- occur due to
  - local lipid metabolism disturbance
  - Altered lipoprotein Content
  - Lymphohistocytic proliferation in skin with secondary deposition of lipids in cells.

Acrodermatitis Enteropathica "AEP" [2]

It is rare, with autosomal recessive inheritance due to mutations in the gene that encodes the zinc transporter SLC39A4 which is expressed in the intestine & kidney.

The normal serum Zn level = 100-125 µg/100 ml. when serum level is below 40 µg/100 ml, AEP develops.

Clinical features

It starts in infancy, 4-6 weeks after weaning or earlier if the infant is not given breast milk. It is characterized by:

1. ***Cutaneous lesions*** (Figs 68-70):
   - Vesiculobullous eruptions with erythema, scaling and crustation affecting periorificial areas (mouth, nose, and anogenital regions) and distal portions of extremities. 2ry candidal infection is common.
   - Chronic paronychia with dystrophic nails.
   - Diffuse hair thinning or total alopecia.

2. ***Diarrhea.***
3. ***Other findings*** may occur as growth retardation, delayed sexual maturity, stomatitis, conjunctivitis with photophobia.

Histopathology: Pallor of the upper part of epidermis due to the presence of clear cells. Diffuse parakeratosis and subcorneal vesicles may be present above the pale epidermal cells.

Pathogenesis: There is decrease in intestinal Zn absorption probably due to the lack of a Zn-binding ligand in small intestine, essential for Zn absorption. This ligand is present in the human milk but not in cow's milk. So, AEP appears after weaning.

Treatment

- 8-hydroxyquinolines → ↑ Zn absorption.
- Zn sulphate 2 mg/kg/day cures the manifestations within 1-2 weeks. Prolonged therapy up to adult age is necessary.

17 Mention the defect in

1 Congenital erythropoietic porphria

it is autosomal recessive inheritance due to deficiency in uroporphyrinogen III synthetase → ↑ uroporphyrin I and coproporphin I

2 Familial hyper cholesterolaemia

it is common, autosomal dominant disease - with ↑ in LDL due to ↓ in LDL receptors → so ↑ T plasma cholesterol with normal TGs level.
A few pt have in association mild ↑ TGs

3 Acrodermatitis enteropathica

It is rare, autosomal recessive inheritance due to mutations in the gene encodes zin transporter SLC39A4

which expressed in the intestine & kidney

- normal Zn serum level 100-125 µg/100 ml
- if ↓ below 40 µg/100 mL, AEP develop

3 phenylketnuria

It is a rare autosomal recessive disorder resuet from deficiency of phenylalanine hydroxylase enzyme leading to accomulation of phenylalanine and its metabolites as phenyl pyruvic acid in serum and urine.

4 porphyria cutanea tarda

- most common form of porphyrias
- due to deficiency of uroporphyrinogen III decarboxylase.
- In Familial PCT ⇝ enzyme deficient in Liver, erythrocytes, and other tissues

*It is autosomal dominant trait in heterozygous individuals -
in homozygous " → develop hepatoerythropoietic porphyria
- In sporadic pCT → enzyme deficient in Liver only
* it is inherited autosomal recessive trait

5 Alkaptonuria

It is rare autosomal recessive disorder
- caused by absence of homogentisic oxidase in the liver and kidney
- accumulation of homogentisic acid
- mainly in fibrous & cartilaginous tissues
- when homogentisic acid polymerize gives brownish black "ochre" pigment deposition & disease ochronosis.

Metabolic ...

Q2. • Compare: Porphyria Cutanea tarda & congenital erythropoietic porphyria & pseudoporphyria.

	Porphyria Cutanea tarda (PCT)	Congenital erythropoietic porphyria	Pseudoporphyria
Etiology	• Any age. Any sex. • Deficiency of uroporphyrinogen decarboxylase (URO-D) enzyme leading to accumulation of uroporphyrin.	• is a hereditary porphyria [illegible] porphyria and is autosomal recessive with incomplete penetrance. • ↓ of ferrochelatase → accumulation of protoporphyrin in RBCs → phototoxic reaction.	• Any age. Any race. [illegible] age [illegible] years. • No demonstrable porphyrin abnormalities. • After use of nalidixic acid. • Furosemide, naproxen, aspirin, tetracyclines & sulfonylureas.
Clinical Picture	● Fragility & blistering (may be painful) in exposed areas. Bullae may crust & resolve → atrophic scars with hypo or hyperpigmentation → fine scale → scarring alopecia. ● Minor trauma of hands → sharply marginated erosions. ● Hypertrichosis of face. ● Photo-induced onycholysis. ● Melasma like hyperpigmentation. ● Morphea like plaques of hands & upper trunk.	● The condition starts at the age of 2-5 yrs. ● Severe pain on light-exposed areas, lasting few hours or days on exposure to sunlight. ● Most pt have no physical signs. ● Some may have oedema, erythema, bullae, erosions, purpuric lesions or small pitted scars on the forehead & cheeks.	● Skin fragility, erythema & the appearance of tense bullae & erosions on sun-exposed areas.
Histopathology	1. Homogenous material is seen within vessel walls of the upper dermal & papillary vascular plexus. 2. It PAS +ve, diastase resistant & contains protein polysaccharide complex, lipids & tryptophan. 3. Bullae are subepidermal, split occurring in the lamina lucida leaving the dermal papillae protruding into the blister cavity (festooning). 4. IF → Immunoglobulin in the same vascular distribution & DEJ (mainly IgG).	1. Endothelial damage & deposition of PAS +ve diastase resistant hyaline material in the walls of blood vessels of the upper dermal & papillary vascular plexuses. 2. IF shows IgG in a similar distribution.	1. Subepidermal bulla with vessel changes & fibrosis in the dermis. 2. IF → deposition of IgG in vessel walls in the dermis & less deposition of C3, IgM, IgA. 3. +ve for plasma porphyrins.
Investigations	1. Skin biopsy. 2. CBC. 3. Liver enzymes. 4. Immunofluorescent. 5. PCR for hepatitis C.	1. The same + 2. Appearance of coproporphyrin in the urine. 3. Liver biopsy.	• The same.
Treatment	● Opaque sunscreens. ● Stop of alcohol or estrogen therapy. ● Treatment of hepatitis C. ● two specific therapy: ● low-dose antimalarials (chloroquin). ● Venesection.	● Sun avoidance & use of opaque sunscreens. ● Acute attacks are treated ē fans & cold water & hospital admission for light avoidance & analgesia ē opiates. ● Chronic cases ē oral β-carotene [illegible] daily (30mg in children). ● NB-UVB in early spring.	1. Stop drug that causes (pseudoporphyria). 2. Opaque sunscreens (titanium oxide or zinc oxide-based sunscreen). ● N-acetylcysteine 200mg four times daily. & 400mg twice daily. ● dialysis

Q10:/ ... & congenital erythropoietic por... " " " & pseudoporphyria?

	Porphyria Cutanea tarda (PCT)	congenital erythropoietic porphyria	Pseudoporphyria
Etiology:	• Any age. Any sex. • Deficiency of uroporphyrinogen decarboxylase (URO D) enzyme leading to accumulation of uroporphyrin.	porphyria characterized porphyria. it is autosomal dominant with incomplete penetrances ↓ of ferrochelatase → accumulation of protoporphyrin in RBCs → photo toxic reaction.	Any sex. Any race. age (min age 30 years) • No demonstrable porphyrin abnormalities • After use of nalidixic acid. • Furosemide, naproxen, aspirin, tetracyclines & sulphonylureas.
Clinical Picture.	• Fragility & blistering (may be painful) in sun exposed areas, bullae may crust & resolves ⇒ atrophic scars with hypo or hyper pigmentation → fine scalp → scarring alopecia • Minor trauma of hands → sharply marginated erosions • Hypertrichosis of face • Photo-induced onycholysis • Melasma-like hyperpigmentation • Morphea like plaques of hands & upper trunk	• The condition starts at the age of 3-5 yrs. • Severe pain on light exposed areas, lasting few hours or days on exposure to sunlight. • Most pt. have no physical signs. • Some may have oedema, erythema bullae, erosions, purpuric lesions or small punched scars on the forehead & cheeks.	• ↑ skin fragility; erythema & the appearance of tense bullae & erosions on sun exposed skin.
Histopathology	1. Homogenous material is seen within vessel walls of the upper dermal & papillary vascular plexus. 2. It PAS +ve, diastase resistant & contains protein polysaccharide complex, lipids & tryptophan. 3. Bullae are subepidermal - split occurring in the lamina lucida leaving the dermal papilla protruding into the blister cavity (Clefting) 4. IF → Immunoglobulin in the same vascular distribution & DEJ (mainly IgG).	1. Endothelial damage & deposition of PAS +ve diastase resistant hyaline material in the walls of blood vessels of the upper dermal & papillary vascular plexuses. 2. IF shows IgG in a similar distribution.	1. Subepidermal bulla with vessel changes & Fibrosis in the dermis. 2. IF → deposition of Ig G in vessel walls in the dermis & less deposition of C_3, IgM & IgA 3. +ve for plasma porphyrins
Investigations	• Skin biopsy • CBC • liver enzymes. • Immunofluorescent. • PCR for hepatitis C	The same + Appearance of copropor-phyrin in the Urine. • liver biopsy	The same
Treatment	• Opaque Sunscreens. • Stop of alcohol or estrogen therapy. • Treatment of hepatitis C. • two specific therapy:- • low-dose antimalarials (chloroquine). • Venesection.	• Sun avoidance & used of opaque sunscreens. • Acute attacks are treated c' fans & cold water & hospital admission for light avoidance & analgesia + opiates. • Chronic cases c' oral β-Carotene 180mg daily (30mg in children) • NB. UVB in early spring.	• Stop drug that causes (pseudoporphyria) • Opaque sunscreens/titanium oxide or zinc oxide-based sunscreen • N-acetylcysteine 200mg four times daily. (a) 600mg twice daily. • dialysis

	the upper dermal & papillary vascular plexus. ● It has PAS +ve diastase resistant & contains protein polysaccharide complex, Igm & Igm fibrin. ● Bullae are subepidermal - split occurring in the lamina lucida losing the dermal papilla protruding into the blister cavity (ballooning). ● IF → Linear Igm in the same vascular distribution & DEJ (mainly IgG).	of blood vessels of the upper dermal & papillary vascular plexuses. 2. IF shows IgG in a similar distribution
Investigations	● Skin biopsy ● CBC ● Liver enzymes ● Immunofluorescent ● PCR for hepatitis C	● The Same + ● Appearance of coproporphyrin in the Urine. ● Liver biopsy
Treatment	● Opaque Sun screens. ● Stop of alcohol or estrogen therapy. ● Treatment of hepatitis C. ● Two specific therapy:	● Sun avoidance & use of opaque sunscreens. ● Acute attacks are treated c' fans & cold water & hospital admission for light avoidance & analgesia